

IT IS CLAIMED:

5 SUB 7
A3
1. A method of administering a therapeutic compound to a cell expressing P-glycoprotein, comprising preparing a conjugate composed of (i) a carrier; (ii) a folate ligand attached to the carrier; and (iii) a therapeutic agent associated with the carrier; and administering the conjugate to a subject.

10 2. The method of claim 1, wherein said preparing includes preparing a conjugate where the carrier is a natural or synthetic polymer.

15 3. The method of claim 1, wherein said preparing includes preparing a conjugate where the carrier is a protein or peptide macromolecule.

20 4. The method of claim 1, wherein said preparing includes preparing a conjugate where the carrier is a liposome having a surface coating of hydrophilic polymer chains and the folate ligand is attached to a distal end of the polymer chains.

25 5. The method of claim 4, wherein the polymer is polyethyleneglycol having a molecular weight of at least about 3,500 Daltons.

30 6. The method of claim 1, wherein said preparing includes preparing a conjugate where the therapeutic agent is a chemotherapeutic drug.

35 7. The method of claim 1, wherein said preparing includes preparing a conjugate where the therapeutic agent is an anthracycline antibiotic.

8. The method of claim 7, wherein the anthracycline antibiotic is selected from the group consisting of doxorubicin, daunorubicin, epirubicin idarubicin, mitoxantrone and an anthraquinone drug.

9. A method of administering to a cell a therapeutic compound which in free form does not accumulate in the cell, comprising,

preparing liposomes composed of (i) vesicle-forming lipids and including a vesicle forming lipid derivatized with a hydrophilic polymer chain having a free distal end, (ii) a folate ligand attached to the free distal end of at least a portion of the hydrophilic polymer chains, and (iii) a therapeutic agent entrapped in the liposomes; and

administering the liposomes to a subject; whereby accumulation of the compound in the cell is achieved in an amount sufficient for cell cytotoxicity.

10. The method of claim 9, wherein said preparing includes preparing liposomes where the hydrophilic polymer is polyethylene glycol having a molecular weight of at least about 3,500 Daltons.

11. The method of claim 9, wherein said preparing includes preparing liposomes where the therapeutic agent is an anthracycline antibiotic.

12. The method of claim 11, wherein the anthracycline antibiotic is selected from the group consisting of doxorubicin, daunorubicin, epirubicin idarubicin, mitoxantrone and an anthraquinone drug.

13. A composition for administration of a therapeutic compound to a multi-drug resistant cell in a person suffering from cancer, comprising

a carrier molecule; at least one folate ligand attached to the carrier molecule; and

a therapeutic compound associated with the carrier, wherein said composition is effective to achieve accumulation of the therapeutic compound in the cell in an amount sufficient to be cytotoxic.

14. The composition of claim 13, wherein the carrier is a natural or synthetic polymer.

15. The composition of claim 13, wherein the carrier is a protein or peptide macromolecule.

16. The composition of claim 13, wherein the carrier is a liposome having a surface coating of hydrophilic polymer chains and the folate ligand is attached to a distal end of the polymer chains.

17. The composition of claim 16, wherein the hydrophilic polymer is polyethylene glycol having a molecular weight of at least about 3,500 Daltons.

18. A liposome composition for administration of a therapeutic compound to a multi-drug resistant cell in a person suffering from cancer, comprising

liposomes composed of vesicle-forming lipids and including a vesicle forming lipid derivatized with a hydrophilic polymer chain having a free distal end,

a folate ligand attached to the free distal end of at least a portion of the hydrophilic polymer chains, and

a therapeutic agent entrapped in the liposomes,

wherein said composition is effective to achieve accumulation of the therapeutic compound in the cell in an amount sufficient to be cytotoxic.

19. The composition of claim 14, wherein the hydrophilic polymer is polyethylene glycol having a molecular weight of at least about 3,500 Daltons.

20. The composition of claim 18, wherein the therapeutic agent is an anthracycline antibiotic.

21. The composition of claim 20, wherein the anthracycline antibiotic is selected from the group consisting of doxorubicin, daunorubicin, epirubicin idarubicin, mitoxantrone and an anthraquinone drug.